Docket No.: PF-0041-4 CON

Response Under 37 C.F.R. 1.116 - Expedited Procedure
Examining Group 1647

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By: _____ Printed: Lisa McDill

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of: Coleman et al.

Title:	POLYNUCLEOTIDES ENCODING THROMBIN RECEPTOR HOMOLOGS		
Serial No.:	09/997,522	Filing Date:	November 28, 2001
Examiner:	Landsman, R.S.	Group Art Unit:	1647

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REPLY BRIEF ON APPEAL

Sir:

I. INTRODUCTION

This is Appellants' Reply Brief on Appeal (submitted in triplicate) in response to the Examiner's Answer dated September 9, 2003 ("the Examiner's Answer") in the above-identified application (the Coleman '522 application).

On page 2 of the Examiner's Answer the Examiner states that the Appellants "provide a statement in the brief that the claims stand or fall together" (Examiner's Answer, page 2, § 7). The claims stand or fall together only with respect to issues 1 and 2. With respect to each of issues 3

through 10, different subgroups of the claims are grouped together for purposes of the Appeal, as indicated in the Brief on Appeal of June 25, 2003 (at page 5, § (7)), and as indicated in the Examiner's Answer under the "Grounds of Rejection" for each issue on appeal at, for example, pages 5, 7, 8, 10, 11, and 12.

In addition, in the Examiner's Answer the Patent Examiner:

(1) maintained the rejection of the claims on appeal under 35 U.S.C. § 101 on the grounds that the claimed polynucleotides are allegedly not supported by a specific and substantial credible utility,

(2) maintained the rejection of the claims on appeal under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because of the invention's alleged lack of utility,

(3) maintained the rejection of claims 3, 6, 7, 9, 12, 13, and 58, on appeal, under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement of the claimed polynucleotides "variants" and "fragments,"

(4) maintained the rejection of claims 3, 6, 7, 9, 12, 13, and 58, on appeal, under 35 U.S.C. § 112, first paragraph, for alleged lack of written description/possession of the claimed polynucleotide "variants" and "fragments,"

(5) maintained the rejection of claims 4, 5, and 57, on appeal, under 35 U.S.C. § 101, for alleged statutory double patenting over claims 1 and 3 of prior U.S. Patent No. 5,686,597,

(6) maintained the rejection of claims 3, 4, 5, 12, 13, and 57, on appeal, for alleged obviousness-type double patenting over claim 1 of U.S. Patent No. 5,869,633,

(7) maintained the rejection of claims 3, 4, 5, 12, 13, and 57, on appeal, for alleged obviousness-type double patenting over claims 1 and 3 of U.S. Patent No. 5,686,597,

(8) maintained the rejection of claim 6, on appeal, for alleged obviousness-type double patenting over claim 2 of U.S. Patent No. 5,686,597,

(9) maintained the rejection of claims 9 and 10, on appeal, for alleged obviousness-type double patenting over claim 6 of U.S. Patent No. 5,686,597, and

(10) maintained the rejection of claims 6 and 7, on appeal, for alleged obviousness-type double patenting over claims 4 and 5 of U.S. Patent No. 5,686,597.

II. ISSUES 1 & 2 -- UTILITY REJECTIONS

A. Overview of Utility Rejections

In the rejections of the claimed invention for alleged lack of utility, the Examiner does not disprove the following:

1) that the claimed polynucleotide of SEQ ID NO:1, encoding the TRH polypeptide having the amino acid sequence of SEQ ID NO:2, is expressed in humans; and

2) that all, or almost all, polynucleotides expressed in humans have specific and substantial utility for measuring undesired side effects of drug candidates in toxicological testing.

It follows that the claimed invention is, by **more** than a reasonable probability, useful. There is no dispute that the Appellants need show no more than a reasonable probability that the claimed invention is useful to meet the requirements of 35 U.S.C. § 101 and § 112, first paragraph.

The Examiner never assails or even addresses this compelling logic. The Examiner continues to insist that the Appellants prove not only reasonable probability of utility, **but also** the biological or physical function of the claimed invention.

Nothing in the law requires the Appellants to prove biological function, and the Examiner does not point to anything in the law suggesting such a requirement. Indeed, the only law on this point is to the contrary: it is settled law -- and the Examiner does not rebut this -- that how an invention works (that is, its function) is utterly irrelevant to the utility analysis. In short, the entirety of the Examiner's argument is based on the confusion between, and improper equation of, use and function.

The Examiner apparently would rely on *In re Kirk* for the proposition that the Appellants must demonstrate biological function. *Kirk* requires no such thing. Indeed, *Kirk* is completely consistent with the requirement that the Appellants need only show utility of the claimed invention to reasonable probability. In *Kirk*, the applicant could not show reasonable probability because the only fact alleged by the applicant was that the claimed invention is a steroid. Because so many steroids -- indeed most of them -- have absolutely no use whatsoever, it followed that the applicant had not shown a reasonable probability of utility.

Application of the same logic to this case -- which the Examiner refuses to do -- yields a completely different result. In this case, the Appellants have identified the claimed invention as a member of a much better defined and narrower group: polynucleotides which encode proteins expressed in humans. As demonstrated above, because polynucleotides encoding proteins expressed in humans are predominantly useful, the Appellants can state with great confidence that the claimed invention is useful. How the invention actually works is utterly irrelevant to the analysis.

B. Responses to Specific Arguments by the Examiner

1. The Examiner contends on page 13 of the Examiner's Answer that "[t]he basis that the receptor encoded for by the polynucleotide of the present invention (or its transmembrane domains and intracellular loops) is only known to be homologous to thrombin receptors . . . is not predictive of a use." The Examiner confuses function with use. These are not synonymous. It is irrelevant whether the SEQ ID NO:1 polynucleotide encodes a polypeptide having the biological activities of a particular subfamily of T7G proteins. The point for the purposes of the utility standard is that the polynucleotide encoding TRH, as a polynucleotide expressed in humans, is indeed useful for toxicology testing, drug discovery, and disease diagnosis.

2. On page 13 of the Examiner's Answer, the Examiner asserts that the claimed polynucleotides have no well-established use in drug development, toxicology studies, or disease diagnosis. The Examiner states that "the Declaration under 37 CFR 1.131 by Lars Michael Furness (Furness Declaration) makes it clear that GPCRs (T7Gs) are targets of many current drug treatments. Again, simply knowing that the protein of the present invention is a GPCR is not sufficient to establish a specific or substantial utility" (Examiner's Answer, page 13). Not so. The claimed polynucleotides can be used for toxicology testing in drug discovery regardless of whether the protein itself is a drug target. Monitoring the expression of the claimed polynucleotides gives important information on the potential toxicity of a drug candidate that is specifically targeted to any other polynucleotide, or to a polypeptide encoded by such a polynucleotide, regardless of the disease association or biological function of the claimed polynucleotides. The claimed polynucleotides are useful for measuring the toxicity of drug

candidates specifically targeted to **other** polynucleotides and polypeptides, regardless of any possible utility for measuring properties of the claimed polynucleotides themselves.

3. On pages 13-14, the Examiner takes issue with Appellants' assertion that membership in a class of useful products can be proof of utility. The Examiner asserts that "Applicants have not identified a specific class of compounds to which the present invention belongs. It appears that Applicants are comparing 'class' to 'the GPCR superfamily.' GPCRs are a diverse superfamily of proteins" (Examiner's Answer, page 13). As discussed in the Brief on Appeal of June 25, 2003, the SEQ ID NO:2 polypeptide (encoded by the SEQ ID NO:1 polynucleotide) could reasonably be considered to belong to the class of polypeptides consisting of T7Gs (GPCRs) based on its structural homology to a known member of this class (e.g., thrombin receptor HUMTHRR). Furthermore, since all of the members of this class are useful as, for example, G-protein coupled receptors that function in signal transduction, a skilled artisan would reasonably conclude that the SEQ ID NO:2 polypeptide was likewise useful. It is irrelevant whether the class to which the SEQ ID NO:2 polypeptide belongs is a diverse superfamily or a less-diverse family, as long as all or most of the members of the class are useful. Since all of the members of the diverse superfamily of GPCRs are useful, one would reasonably conclude that the SEQ ID NO:2 polypeptide is useful.

4. The Examiner argues on pages 14-15 that the utilities disclosed in the specification for gene and protein expression monitoring are not specific. The Examiner's argument amounts to nothing more than the Examiner's disagreement with the Furness Declaration and the Appellants' assertions about the knowledge of a person of ordinary skill in the art, and is tantamount to the substitution of the Examiner's own judgment for that of the Appellants' expert. The Examiner must accept the Appellants' assertions to be true. The Examiner is, moreover, wrong on the facts because the Furness Declaration demonstrates how one of skill in the art, reading the specification at the time the parent of the instant application was filed (June 6, 1995), would have understood that specification to disclose the use of the claimed polynucleotides in gene expression monitoring for toxicology testing, drug development, and the diagnosis of disease (See the Furness Declaration at, e.g., ¶¶ 10-13).

5. The Examiner states on page 14 that "in the absence of a knowledge of the biological activity of the encoded protein, or in the absence of a knowledge as to what subfamily of receptor this

protein belongs, it would not be clear to the artisan how to interpret the toxicology findings." Dr. Furness in his Declaration states, and one of skill in the art would know, that "good drugs are not only potent, they are specific. This means that they have strong effects on a specific biological target and minimal effects on all other biological targets" (Furness Declaration, ¶ 10 at pages 8-9). Thus, if the expression of a particular polynucleotide is affected in any way by exposure to a test compound, and if that particular polynucleotide (or the polypeptide encoded by it) is not the specific target of the test compound (e.g., if the test compound is a drug candidate), then the change in expression is an indication that the test compound has undesirable toxic side effects. It is important to note that such an indication of possible toxicity is specific not only for each compound tested, but also for each and every individual polynucleotide sequence.

The Examiner continues this argument by stating that "if a drug had no effect on expression levels of the gene of the present invention, this, again, would provide no valuable information to the artisan as to the specific or substantial role of the gene or encoded protein" (Examiner's Answer, page 14). The Examiner seems to be missing the point. The asserted utility of the claimed invention is not to provide information as to the specific or substantial role of the gene or encoded protein. It is to provide information as to the possible toxicity of drug candidates targeted to **other** genes, and their encoded proteins. As discussed above (e.g., in § II.B.2), the claimed polynucleotides are useful for measuring the toxicity of drug candidates specifically targeted to polynucleotides and polypeptides **other than** the claimed polynucleotides (and their encoded polypeptides). The effect of any particular drug candidate on the expression of any particular naturally occurring polynucleotide will be **specific** to both the drug candidate and the polynucleotide sequence. Such a toxicology test using an expressed polypeptide will differ from a toxicology test using any other expressed polynucleotide. Therefore, the asserted utility of the claimed polynucleotide in toxicology testing is credible, specific, and substantial.

6. The Examiner argues on page 15 that use as a control for toxicology testing is not a specific, substantial and credible utility, and therefore not a "well established" utility, because "all nucleic acids and genes are useful in toxicological testing (this is analogous to 2D-PAGE gels). Therefore, this is a utility which is non-specific and would apply to virtually every member of a general class of materials, such as proteins or DNA" (Examiner's Answer, page 15). The Examiner doesn't point to any law,

however, that says a utility that is shared by a large class is somehow not a utility. If all of the class of expressed polynucleotides can be so used, then they all have utility. The issue is, once again, whether the claimed invention has any utility, not whether other compounds have a similar utility. Nothing in the law says that an invention must have a "unique" utility. Indeed, the whole notion of "well established" utilities **presupposes** that many different inventions can have the exact same utility. If the Examiner's argument was correct, there could never be a well established utility, because you could always find a generic group with the same utility!

Furthermore, the Examiner is factually incorrect in stating that any new polynucleotide could be used in a microarray as a control for toxicology testing. The property of the claimed polynucleotides that makes them useful as controls for toxicology testing is their expression in naturally occurring cells. A polynucleotide having a random, non-naturally occurring sequence would most likely not be useful as a control for toxicology testing.

7. The Examiner questions whether the claimed invention is substantial by stating that "if the claimed compound is only useful as [part of] a larger mixture, then it is the larger mixture that possess the utility" (Examiner's Answer, page 15). However, the Examiner ignores the fact that the claimed polynucleotides are also useful by themselves. It is useful to know whether the expression of the claimed SEQ ID NO:1 polynucleotide is altered by a drug candidate, irrespective of whether the expression of any other polynucleotides are also tested. The Examiner is incorrect in implying that the "claimed compound is only useful as [part of] a larger mixture."

C. Summary

It is true that just about any expressed polynucleotide will have use as a toxicology control, but Appellants need not argue this for the purposes of this case. Appellants argue only that this particular claimed invention could be so used, and have provided the Declaration of Furness to back this up. The Examiner is completely wrong to characterize Appellants' argument re: utility of a polynucleotide as a toxicology control somehow requires the person using the invention to do further research to identify the biological function or disease association of that polynucleotide. The point is not whether the invention is, in any given toxicology test, differentially expressed. The point is that the invention provides a useful

measuring stick regardless of whether there is or is not differential expression. That makes the invention useful today, in the real world, for real purposes having nothing to do with further characterization of the invention itself.

III. ISSUE 3 -- ENABLEMENT REJECTION OF VARIANTS AND FRAGMENTS

In maintaining the rejection of the claimed polynucleotide variants and fragments for alleged lack of enablement, the Examiner continues to focus on a misguided requirement for knowledge of precise biological function. The Examiner asserts that "the substitution of one amino acid, or, more likely, the insertion or deletion of 1-5 residues into SEQ ID NO:2, for example, would encompass proteins with functions other than those predicted for SEQ ID NO:2, which itself has no function" (Examiner's Answer, pages 15-16). The Examiner is incorrect in asserting that Appellants have failed to demonstrate that TRH has G-protein coupled seven transmembrane receptor (T7G) activity. A skilled artisan would **reasonably** conclude that the SEQ ID NO:2 polypeptide has T7G activity, based on homology to known T7G proteins. Such a conclusion is supported by the teachings of Brenner et al. (Proc. Natl. Acad. Sci. USA, 1998, 95:6073-6078; of record), which speaks to the **general applicability** of using sequence homology as low as 30% over 150 amino acid residues to indicate protein homology, and Bork (Genome Res., 2000, 10:398-400; of record), which teaches that the prediction of functional features by homology has a 90% accuracy rate (Table 1 of Bork).

With respect to naturally occurring sequences, the Examiner states that "it would not be predictable to the artisan which proteins having these substitutions, insertions or deletions would be naturally occurring variants of SEQ ID NO:2 and which would be similar, but not considered a naturally occurring variant" (Examiner's Answer, page 16). This statement completely ignores Appellant's arguments in the Brief on Appeal of June 25, 2003, which points out methods described in the specification for obtaining polynucleotides encoding polypeptides comprising naturally occurring sequences, and polynucleotides comprising naturally occurring sequences:

> For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the Specification

of the instant application. See, e.g., page 9, lines 7-20. (Brief on Appeal, June 25, 2003; page 31)

Thus, one of skill in the art could routinely obtain the claimed polynucleotides comprising naturally occurring sequences, or encoding polypeptides comprising naturally occurring sequences, without undue experimentation.

In addition, the Examiner asserts that one "cannot determine how one would distinguish, merely by examination of the protein, whether a protein were the result of expression of a different allele, or alternatively, were merely one of a number of ultimate species that might be obtained by the expression of SEQ ID NO:1" (Examiner's Answer, page 17). However, the question is not whether one could distinguish, merely be examination of a protein, whether the protein was the result of expression of a different allele. The question is whether one of skill in the art would reasonably understand how to make and use the invention. A skilled artisan could routinely make the claimed polynucleotides encoding polypeptides comprising naturally occurring sequences by, for example, hybridization and/or PCR techniques that were well known to those skilled in the art at the time the subject application was filed. One of skill in the art could routinely use the claimed polynucleotides as, for example, hybridization probes to detect full-length human variants of the SEQ ID NO:1 polynucleotide. Since one of skill in the art would reasonably understand how to make and use the claimed invention, without undue experimentation, the enablement requirement of 35 U.S.C. § 112, first paragraph, has been met.

The Examiner asserts that Appellants do not specifically address the issue of the term "naturally occurring variant" reading on allelic variants of the protein of SEQ ID NO:2 (Examiner's Answer, page 16). Allelic variants which are within the scope of the claimed polynucleotides are a subset of the claimed polynucleotide variants. Therefore, since the claimed polynucleotide variants meet the enablement requirement of 35 U.S.C. § 112, first paragraph, allelic variants which are within the scope of the claimed polynucleotides also meet the enablement requirement of 35 U.S.C. § 112, first paragraph.

With respect to "thrombin-binding fragments," the Examiner asserts that "Applicants have not provided any guidance or working examples as to which regions of the protein of SEQ ID NO:2 is responsible for its function, especially in light of the fact that the full-length protein has no utility"

(Examiner's Answer, page 16). However, as discussed above and in the Brief on Appeal of June 25, 2003, the full-length SEQ ID NO:2 polypeptide has specific, substantial, and credible utilities. Furthermore, the question is not whether there are regions of SEQ ID NO:2 which are responsible for its biological function. The question is whether one of skill in the art would reasonably understand how to make and use the invention. A skilled artisan could routinely make the claimed polynucleotides encoding thrombin-binding fragments of SEQ ID NO:2 by, for example, screening polypeptide fragments of SEQ ID NO:2 for thrombin-binding activity. The claimed polynucleotides encoding thrombin-binding fragments of SEQ ID NO:2 could be used, for example, to produce polypeptides for binding to and/or purifying thrombin. There is no need to predict "which regions of the protein of SEQ ID NO:2 is responsible for its function" because the claimed polynucleotides could be obtained by routine methods known in the art.

Furthermore, it is clear that, based on the arguments presented in the Brief on Appeal, the Declaration of Furness, and above, the claimed invention has at least one patentable utility that was well established at the time of filing of the parent of the instant patent application (June 6, 1995). One of ordinary skill in the art would know how to use the claimed invention as, for example, a toxicology control in drug discovery. The Examiner has completely ignored this use in evaluating the enablement of the claimed polynucleotides. There is no evidence that a skilled artisan would doubt that the claimed polynucleotides could be used for conducting toxicology tests of compounds during drug discovery.

For at least the above reasons and the reasons presented in the Brief on Appeal, reversal of this rejection is requested.

IV. ISSUE 4 -- WRITTEN DESCRIPTION REJECTIONS

A. Overview of Written Description Rejections

Nowhere in the Examiner's Answer does the Examiner offer any evidence that one of ordinary skill in the art would not have understood, from the disclosure in the specification, along with "[w]hat is conventional or well known to one of ordinary skill in the art," that Appellants were in possession of the claimed polynucleotide variants and fragments. The Examiner instead states that "the structure of

naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1 and 2, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and polypeptides and, therefore, conception is not achieved until reduction to practice has occurred" (Examiner's Answer, pages 17-18).

The Examiner's position is contrary to the Patent and Trademark Office's own written description guidelines ("Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001), which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. **What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.** [footnotes omitted; emphasis added]

Here, there simply is no requirement that the claims recite the sequences of particular variants and fragments because the claims already provide sufficient structural definition of the claimed subject matter. That is, the claimed variants and fragments are defined in terms of SEQ ID NO:1 and SEQ ID NO:2. Because the claimed variants and fragments are defined in terms of SEQ ID NO:1 and SEQ ID NO:2, the precise chemical structure of every variant within the scope of the claims can be discerned. Furthermore, there is no requirement that the claims explicitly recite the sequence of every variant and fragment within the scope of the claims. The Examiner's position is nothing more than a misguided attempt to require Appellants to unduly limit the scope of their claimed invention.

B. Responses to Specific Arguments by the Examiner

1. The Examiner asserts on page 17 of the Examiner's Answer that "[t]here is no definition of what defines a variant of SEQ ID NO:2, especially in light of the fact that the protein of SEQ ID NO:2 lacks utility." Matters related to the utility of polynucleotides encoding the SEQ ID NO:2 polypeptide

are addressed above (e.g., in § II) and in the Brief on Appeal of June 25, 2003. Furthermore, the Examiner is incorrect in asserting that there is no definition of what defines a variant of SEQ ID NO:2. Variants of SEQ ID NO:2 are described in the specification at, for example, page 4, lines 30-32; page 5, lines 22-25; and page 5, line 30 to page 6, line 11.

2. The Examiner asserts that Appellants do not specifically address the issue of the term "naturally occurring variant" reading on allelic variants of the protein of SEQ ID NO:2 (Examiner's Answer, page 17). Allelic variants which are within the scope of the claimed polynucleotides are a subset of the claimed polynucleotide variants. Therefore, since the claimed polynucleotide variants meet the written description requirement of 35 U.S.C. § 112, first paragraph, allelic variants which are within the scope of the claimed polynucleotides also meet the written description requirement of 35 U.S.C. § 112, first paragraph.

3. The Examiner states on page 18 of the Examiner's Answer that "[t]he common attributes of the genus are not described and the identifying attributes of individual alleles, other than SEQ ID NO:1, or the protein of SEQ ID NO:2, are not described." This is incorrect. The claimed polynucleotide variants are described in terms of their common structural features (e.g., differing from the amino acid sequence of SEQ ID NO:2 by a substitution of one amino acid residue and/or an insertion of 1-5 amino acid residues and/or a deletion of 1-5 amino acid residues), and in terms of other features such as occurrence in nature.

4. The Examiner asserts that the specification does not provide an adequate written description of the claimed polynucleotide fragments of naturally occurring human variants of SEQ ID NO:1 "[s]ince the naturally occurring variants lack written description" (Examiner's Answer, page 19). This is incorrect. As discussed above and in the Brief on Appeal of June 25, 2003, the specification provides an adequate written description of the recited polynucleotide variants. In addition to this adequate written description, the specification also provides an adequate written description of fragments of the recited polynucleotide variants.

5. The Examiner asserts that "Applicants are defining thrombin-binding fragments as fragments which have the functional characteristic of binding thrombin" (Examiner's Answer, page 19). This assertion ignores the fact that the polynucleotides in question encode "a thrombin-binding fragment of a

polypeptide, wherein the polypeptide **has the amino acid sequence of SEQ ID NO:2**." Therefore, the thrombin-binding fragments are defined not only by the functional characteristic of thrombin binding. The thrombin-binding fragments are also defined by the structural characteristic of being a fragment of the amino acid sequence of SEQ ID NO:2, which has been explicitly disclosed in the specification (e.g., in the Sequence Listing). The combination of functional and structural characteristics provides an adequate written description of the claimed polynucleotides encoding thrombin-binding fragments of SEQ ID NO:2.

C. Summary

The Examiner has asserted that the function and/or sequence of each of the claimed polynucleotide variants and fragments must be provided in order for there to be an adequate written description of the claimed genus. However, this is not true. The Patent Office guidelines state that an adequate written description can be provided by "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, **or** some combination of such characteristics" (P.T.O. Guidelines, *supra*; emphasis added). Therefore, there is no absolute requirement to provide the function and/or sequence of every claimed polynucleotide. The claimed polynucleotides have been described by chemical structure (e.g., relation of the recited polynucleotides to SEQ ID NO:1, relation of the recited polypeptides to SEQ ID NO:2), physical properties (e.g., occurrence in nature of the recited variant sequences), and chemical properties (e.g., immunogenic activity and/or thrombin-binding activity of the recited polypeptide fragments). Therefore, the written description requirement has been met.

For at least the above reasons and the reasons presented in the Brief on Appeal, reversal of this rejection is requested.

V. ISSUE 5 -- STATUTORY DOUBLE PATENTING

In maintaining the rejection of claims 4, 5, and 7 for alleged statutory double patenting over claims 1 and 3 of prior U.S. Patent No. 5,686,597, the Examiner continues to insist that "unless otherwise defined, 'isolated' means the same as 'purified', and 'isolated and purified' is merely

redundant" (Examiner's Answer, page 20, § (e)). Both of the dictionary definitions for "purify" provided by the Examiner in the Examiner's Answer require one to "rid" the product "of impurities" or "of foreign or unwanted elements." In contrast, the third dictionary definition for "isolate" cited by the Examiner in the Examiner's Answer recites "to obtain in an uncombined form." Therefore, as stated previously in, for example, the Brief on Appeal of June 25, 2003, the term "purified" would encompass the separation of a pre-existing object from other materials while the term "isolated" could additionally encompass the production of an object in an environment separate from other materials. Therefore, the terms "purified" and "isolated" are not exactly the same, and the scope of the claims at issue differ from the scope of claims 1 and 3 of prior U.S. Patent No. 5,686,597.

For at least the above reasons and the reasons presented in the Brief on Appeal, reversal of this rejection is requested.

VI. ISSUES 6-10 -- OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

Appellants request that the requirement for submission of Terminal Disclaimers with respect to the '633 and '597 patents be held in abeyance until such time that there is an indication of allowable subject matter. The Examiner has acknowledged that these rejections will be withdrawn upon filing of such Terminal Disclaimers (Examiner's Answer, page 20, §§ (f)-(j)).

VII. CONCLUSION

For all the foregoing reasons and the reasons stated in the Appellants' Brief on Appeal, it is submitted that the Examiner's rejections of the claims on appeal should be reversed.

If the USPTO determines that any additional fees are due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**.

This form is enclosed in triplicate.

Respectfully submitted,

INCYTE CORPORATION

Date: November 6, 2003

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